UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

DIVISION OF
CORPORATION FINANCE

April 26, 2019

Steven Paul, M.D.
Chief Executive Officer, President and Chairman
Karuna Therapeutics, Inc.
33 Arch Street, Suite 3110
Boston, MA 02110

**Re: Karuna Therapeutics, Inc.**
**Draft Registration Statement on Form S-1**
**Submitted March 29, 2019**
**CIK No. 0001771917**

Dear Dr. Paul:

We have reviewed your draft registration statement and have the following comments. In some of our comments, we may ask you to provide us with information so we may better understand your disclosure.

Please respond to this letter by providing the requested information and either submitting an amended draft registration statement or publicly filing your registration statement on EDGAR. If you do not believe our comments apply to your facts and circumstances or do not believe an amendment is appropriate, please tell us why in your response.

After reviewing the information you provide in response to these comments and your amended draft registration statement or filed registration statement, we may have additional comments.

Draft Registration Statement on Form S-1 submitted March 29, 2019

Pipeline Overview, page 2

1. We note your inclusion of "Muscarinic-Targeted Drug Candidate" in your pipeline table on pages 2 and 103. Please expand your disclosure on page 115 to describe your discovery and preclinical development of these programs including, whether preclinical trials have been conducted, and if so, provide a summary of the studies performed and identify any known potential indications. Please note, product candidates should only be included in the table if they are material. If you have not conducted studies relating to these additional product candidates, please remove them from the table or explain the basis for your belief that they are material product candidates. .

Third-Party Clinical Trials Support Xanomelines Development, page 3

2. Please delete your statements indicating xanomeline's efficacy here and in the business section, such as "xanomeline was associated with meaningful dose-dependent improvements;" "trospium was associated with meaningfully fewer cholergic adverse events;" "KarXT has strong clinical and commercial potential;" "Xanomeline has exhibited promising antipsychotic and precognitive effects;" "data suggest xanomeline may improve cognition in patients with AD:" and "Xanomeline has exhibited antipsychotic and precognitive benefits." Safety and efficacy determinations are the exclusive authority of the FDA or alternative foreign regulators. You may provide a summary of the data that you used to draw these conclusions, but not the conclusions or predictions that the product candidates are safe or effective.

3. We note that Xanomeline's side effects resulted in a high rate of discontinuation in the mid- and high-dose cohorts, leading to a substantial reduction of statistical power. Please expand the discussion to quantify the approximate percentage of subjects in the clinical trial that discontinued treatment.

4. We note your statement that cognitive symptoms of patients with AD treated with xanomeline showed improvements compared to placebo as measured by both the ADAS-Cog and the CIBIC+, suggesting that xanomeline can also improve cognition. Please revise to present the data you used to draw this conclusion. In addition, please disclose the sample size in the mid-dose cohort. Please make corresponding revisions to the disclosure in your Business section on page 107.

Our Clinical Trials, page 4

5. Please revise the discussion of your Phase 1 clinical trial to replace the statement relating to "meaningfully fewer cholinergic adverse events" to present the data you used to draw this conclusion. Please make corresponding revisions to the disclosure in your Business section on page 110.

Use of Proceeds, page 76

6. Please revise the discussion to clarify whether you expect to complete each development phase referenced. For example, the first bullet point indicates you expect to fund the completion of your ongoing Phase 2 clinical trial and a planned Phase 3 trial for the treatment of psychosis. Please clarify whether you expect to complete both the Phase 2 and 3 trials or if you expect to complete the Phase 2 trial and begin the Phase 3 trial.

Management's Discussion and Analysis of Financial Condition and Results of Operations
Critical Accounting Policies and Estimates
Determination of the Fair Value of Common Stock, page 97

7. Once you have an estimated offering price or range, please explain to us the reasons for any differences between the recent valuations of your common shares leading up to the

initial public offer and the estimated offering price. This information will help facilitate our review of your accounting for equity issuances including stock compensation.

Xanomeline for the Treatment of Psychotic Symptoms and Agitation in AD, page 106

8. Please clearly disclosure the number of patients out of the 343 that participated in the 225 mg xanomeline arm compared to placebo.

Exclusive Jurisdiction for Certain Actions, page 171

9. We note your restated certificate of incorporations provides that the Court of Chancery of the State of Delaware will be the sole and exclusive forum for any derivative action or proceeding brought on your behalf. Please revise this section, and the risk factor on page 72, to include a discussion regarding whether your exclusive forum provision applies to actions arising under the federal securities laws. In this regard, we note that Section 27 of the Exchange Act creates exclusive federal jurisdiction over all suits brought to enforce any duty or liability created by the Exchange Act or the rules and regulations thereunder.

Exhibits

10. We note your reference to the Wellcome Funding Agreements. Please file these agreements or provide further analysis as to why you are not required to file these agreements as exhibits pursuant to Item 601(b)(10) of Regulation S-K.

General

11. Please supplementally provide us with copies of all written communications, as defined in Rule 405 under the Securities Act, that you, or anyone authorized to do so on your behalf, present to potential investors in reliance on Section 5(d) of the Securities Act, whether or not they retain copies of the communications.

12. Please provide us proofs of all graphics, visual, or photographic information you will provide in the printed prospectus prior to its use, for example in a preliminary prospectus. Please note that we may have comments regarding this material.

You may contact Bonnie Baynes at 202-551-4924 or Angela Connell at 202-551-3426 if you have questions regarding comments on the financial statements and related matters. Please contact Jeffrey Gabor at 202-551-2544 or Suzanne Hayes at 202-551-3675 with any other questions.

Sincerely,

Division of Corporation Finance
Office of Healthcare & Insurance